

Honey as an alternative wound healing therapy: a systematic review of clinical and preclinical evidence (2020–2024)

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ABSTRACT

Wound management remains a significant global public health challenge, contributing to substantial morbidity, mortality, and healthcare costs. Honey has been increasingly investigated as a complementary wound care agent due to its antimicrobial, anti-inflammatory, and wound-healing properties. This systematic review aimed to synthesize and critically evaluate the current evidence on the use of honey as an alternative wound treatment. A systematic review was conducted following PRISMA guidelines. Six electronic databases (Scopus, Nature, ProQuest, EBSCO, SpringerLink, and ScienceDirect) were searched using predefined search terms for studies published between 2020 and 2024. Inclusion criteria encompassed human studies, mixed-methods or quantitative designs, and interventions using honey for wound care. Study quality was assessed using the Joanna Briggs Institute (JBI) critical appraisal tools. From 302 initially identified articles, 16 studies met the inclusion criteria after removing duplicates and screening. The included studies comprised randomized controlled trials, prospective controlled studies, case series, and in vitro investigations. Three themes emerged: i) Honey as a wound-healing therapy, demonstrating antimicrobial, anti-inflammatory, and biofilm-inhibiting properties; ii) Benefits of medical-grade honey (MGH), including accelerated epithelialization, reduced infection rates, and shorter recovery times; and iii) Recommendations for honey as a cost-effective, accessible alternative treatment. The evidence supports honey as a promising adjunctive therapy for wound management, particularly in resource-limited settings. However, the heterogeneity in study designs, honey types, and wound categories limits definitive conclusions. Future large-scale randomized controlled trials with standardized outcomes are needed to establish clinical guidelines for honey-based wound care.

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1. INTRODUCTION

Wounds represent a major global public health burden, affecting an estimated 1–2% of the general population in developed countries and contributing significantly to disability-adjusted life years (DALYs) and healthcare expenditure [1], [2]. Chronic and acute wounds pose challenges, including pain, infection, prolonged morbidity, and reduced quality of life [3]. The economic impact is substantial; wound care costs exceed \$25 billion annually in the United States alone, with a significant additional burden in low- and middle-income countries (LMICs) where access to advanced wound care products is limited [4]–[6].

Wound healing is a complex biochemical process involving inflammation, proliferation, and remodeling phases that require coordinated cellular signaling [3], [7]. Multiple factors influence healing outcomes, including nutritional status, comorbidities (e.g., diabetes mellitus), age, immunological status, and infection [8]. The growing elderly population and rising prevalence of diabetes have substantially increased the burden of chronic wounds, including diabetic foot ulcers and pressure sores, posing particular challenges for healthcare systems worldwide [2], [5], [9].

Poorly healing wounds are also susceptible to bacterial colonization and may progress to sepsis, a life-threatening condition affecting approximately 49 million people and causing 11 million deaths annually [10]. Sepsis is a significant health problem worldwide [4], [11]. Approximately 85% of sepsis cases occur in LMICs, underscoring the disproportionate impact on vulnerable populations [4], [11].

Conventional wound treatments, while effective, are often expensive, associated with adverse effects such as allergic reactions and antimicrobial resistance (AMR), and may be unreliable in underserved areas [3], [12]. The rise of ALMR has created an urgent need for alternative strategies in treating all types of infections in wound management [12], [13]. In this context, honey has emerged as a promising therapeutic agent, with a long history of use in traditional medicine across cultures [14]. Honey possesses antimicrobial, anti-inflammatory, and antiseptic properties, and medicinal-grade honey (MGH) products have been increasingly adopted in clinical wound care [15], [16]. Its affordability, accessibility, and cultural familiarity make it particularly relevant for low-resource settings and community-based wound care [15], [17].

Despite growing evidence, no recent systematic review has comprehensively synthesized clinical and preclinical evidence on honey as a wound healing therapy covering the period 2020–2024. This review aims to address this gap by evaluating the current evidence base, identifying effective honey-based interventions, and providing recommendations for clinical practice, public health policy, and future research.

2. METHOD

2.1. Study design

A systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The review aimed to synthesize evidence on honey use as an alternative wound treatment. The PRISMA framework was applied to ensure a structured and transparent review process.

2.2. Literature search strategy

This systematic review looked at original research findings from six databases: Scopus, Nature, Proquest, EBSCO, Springerlink, and Science Direct. The search was conducted between January and March 2024, covering articles published from January 2020 to December 2024. The following search string was used: ("wound care" OR "wound healing" OR "wound treatment" OR "wound management") AND ("honey" OR "medical grade honey" OR "manuka honey") AND ("alternative treatment" OR "alternative therapy" OR "complementary therapy"). The search was limited to English-language articles that were available in full text, open access, and published between 2020 and 2024.

2.3. Inclusion and exclusion criteria

Inclusion criteria: i) Studies involving human participants or in vitro models relevant to wound care; ii) Interventions involving honey for wound care; iii) Reports on honey as an alternative wound treatment; and iv) Quantitative, qualitative, or mixed methods study designs. Studies involving diverse wound types (surgical, chronic, diabetic, pressure ulcers, infected wounds) were included. Exclusion criteria: i) animal-based wound care studies, ii) studies focusing exclusively on modern wound dressing techniques without honey, and iii) systematic reviews, literature reviews, or editorials. The PRISMA flow diagram outlines the search strategy and study selection process (see Figure 1).

2.4. Risk of bias assessment

Study quality was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Tools, with specific checklists applied according to study design: the JBI checklist for randomized controlled trials, the checklist for case series, and the checklist for analytical cross-sectional studies. Each study was independently appraised by two reviewers (DII and SM), and disagreements were resolved through discussion with a third reviewer (EK).

2.5. Data extraction and analysis

Data extraction used standardized forms to capture study design, setting, participants, intervention details, outcomes, and key results. Four reviewers (EK, DII, SM, DM) independently collected data, resolving disagreements by consensus. Due to substantial heterogeneity in study designs, wound types, honey

types and concentrations, and outcome measures, a quantitative meta-analysis was not feasible. Therefore, analysis relied on narrative synthesis to interpret and organize findings thematically.

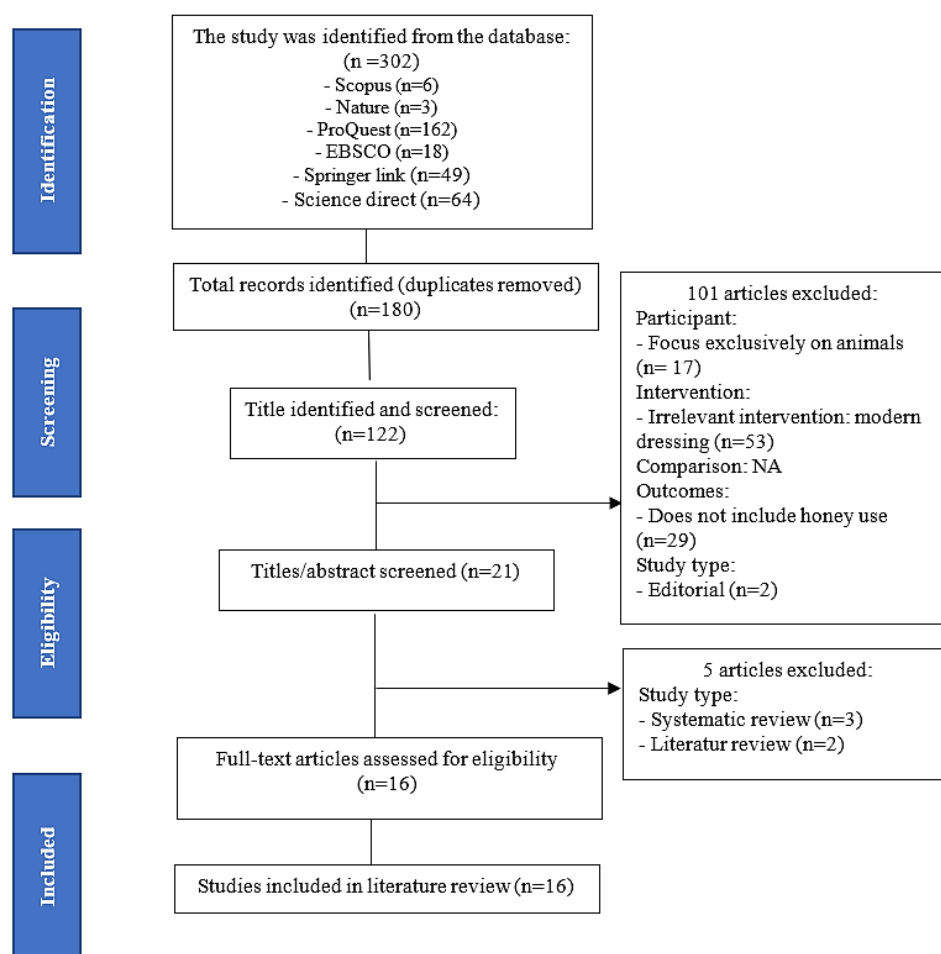


Figure 1. Flow diagram of systematic review

3. RESULTS

A total of 302 articles were identified across six databases, and 180 duplicate articles were removed. Titles and abstracts of 122 articles were screened, resulting in 21 articles deemed eligible. After full-text screening and applying exclusion criteria, 16 studies met the inclusion criteria and were included in the review (Table 1 (see Appendix)) [18]-[32].

The 16 included studies comprised six randomized controlled trials, three prospective studies, four case series, and three in vitro/laboratory studies. Studies covered diverse wound types including surgical wounds (palatoplasty, third molar extraction, caesarean section, pilonidal cyst excision, gingival grafts), chronic wounds (pressure ulcers, infected wounds), and diabetic wounds. Various honey types were investigated, including medical-grade honey (MGH), Manuka honey, chestnut honey, heather honey, and region-specific Nigerian honeys.

3.1. Theme 1: Honey as a wound healing therapy

The review demonstrated that honey is a complex matrix containing over 200 chemical compounds with significant compositional variations depending on geographical origin [32]. Several investigations have found that heather honey has potential as an antibacterial agent for use in wound dressing compositions [30]. A randomized controlled study discovered that iodine and Manuka honey-based dressings can reduce the bacterial load in highly contaminated soft tissue wounds [22]. Local MGH therapy reduced the bacterial burden, resulting in sterile cultures in some instances [26], which prevented bacterial growth and biofilm development [29].

Across the included studies, antimicrobial outcomes varied by honey type and concentration. Manuka honey and MGH products consistently demonstrated broad-spectrum antibacterial activity, while the efficacy of other honey types (e.g., chestnut, heather) was more specific to certain bacterial strains. This heterogeneity in antimicrobial profiles reflects compositional differences influenced by floral source, geographic origin, and processing methods.

3.2. Theme 2: The advantages of medical-grade honey (MGH) in wound healing

Clinical studies demonstrated that honey dressings made substantial differences in wound healing outcomes. Wound care utilizing honey dressings resulted in clinically significant epithelialization of lateral palatal defects in 66.7% of test group participants at two weeks post-surgery [18]. A case series found that MGH provides a moist wound environment, induces autolytic debridement, exhibits anti-inflammatory activity, and promotes angiogenesis and re-epithelialization [25]. MGH demonstrated significantly faster recovery up to day 42 post-caesarean section [23], reduced bacterial burden and infection risk [28], and improved surgical outcomes with shortened recovery time [21]. Notably, the strength of evidence varied across studies. RCTs provided more robust evidence for honey's efficacy in surgical wound healing, while case series offered preliminary support for its use in chronic wound management. In vitro studies elucidated potential mechanisms but have limited direct clinical applicability.

3.3. Theme 3: Recommendations for the use of honey as an alternative wound treatment

The review identified that honey can be used as an alternative wound treatment. A case series study recommends honey as an alternative or complementary therapy in wound healing [25]. Cost considerations are also a reason for using honey, with quantitative studies showing that honey can be a cost-effective and easy-to-use alternative for treating chronic wound infections [26]. This is reinforced by Koloh *et al.* [29], who state that chestnut honey is an alternative treatment for resistant infections and chronic wounds. The ease of use of honey dressings is another reason, as honey is a practical, simple, and affordable method for wound care in various orthopaedic conditions, even with exposed bones or tendons [15]. The findings of this systematic review reinforce medical-grade honey (MGH) as a powerful alternative treatment to replace antibiotics and povidone-iodine, while accelerating healing [23]. Additionally, honey accelerates the wound healing process, leading to a shorter recovery period and reduced post-operative morbidity [20].

4. DISCUSSION

This systematic review provides a comprehensive synthesis of clinical and preclinical evidence on honey as an alternative wound healing therapy published between 2020 and 2024. The findings support honey's efficacy across multiple wound types, with evidence for antimicrobial, anti-inflammatory, and wound-healing-promoting properties. However, the evidence base remains heterogeneous, and several important considerations warrant discussion [33].

4.1. Recommendations for using honey as an alternative wound treatment

Honey alternatives for wound care are becoming the preferred choice for various reasons, including affordability, convenience of use and acquisition, kind of wound, wound length, infection control, and maximum and faster wound healing process. Honey is a natural honey that has naturally occurring antibacterial properties. Over the past few years, honey has been utilized more frequently in contemporary medicine as a "potent agent" in wound healing due to its antibacterial and anti-inflammatory properties. Honey contains several antioxidants, including flavonoids, monophenols, polyphenols, vitamin C, and methylsyngate, which inhibit the amplification of inflammation caused by reactive oxygen species (ROS). These antioxidants are responsible for the method that honey uses to alleviate wound pain [34], [35]. Honey, in addition to being a solution high in sugar, is also a biological wound dressing that contains many bioactive components that can stimulate wound healing through various pathways. Honey can speed up the healing process of wounds by working on the three phases of growth: proliferation, remodelling, and inflammation [7]. Honey is known to enhance the production of collagen, as well as angiogenesis and granulation tissue creation. Additionally, honey boosts wound contraction and promotes epithelialization. In addition to alleviating pain and removing odor from the area, honey also has a debridement effect, meaning it removes debris from the lesion [15]. Allergies to honey are rare, but allergic reactions to honey proteins and allergens are possible.

4.2. Honey as a wound healing therapy

According to this review, honey is a highly complex matrix containing over 200 chemicals with a wide range of compositional variations depending on its origin [32]. Several investigations have found that heather honey has potential as an antibacterial agent for use in wound dressing compositions [30]. A randomized controlled study discovered that dressings containing iodine and Manuka honey can reduce the bacterial load in

severely contaminated soft tissue wounds [22]. Local MGH therapy reduced the bacterial load, in some cases resulting in sterile cultures [26], and inhibited bacterial growth and biofilm production [29].

The findings suggest that altering honey concentration can hinder growth and reduce the number of germs. This notion is based on the fact that chronic and persistent wounds are frequently caused by bacterial colonization of the afflicted tissue. This mechanism can result in bacterial resistance to antimicrobials, both topical and systemic. As a result, this has the potential to raise morbidity and mortality rates. Honey has been shown to include antibacterial and anti-inflammatory effects [14], [36]. Honey's capacity to heal wounds can be attributed to several mechanisms, including its anti-inflammatory and antioxidant properties. Honey not only encourages re-epithelialization and angiogenesis, but it also stimulates skin cell growth and boosts the immune system. Honey's distinct properties, including high osmolality, low water content, and acidic pH, when combined with specific chemicals such as hydrogen peroxide, phenolic compounds, methylglyoxal, and bee defensin-1 peptides, have a direct impact on bacterial growth and survival. Furthermore, honey has indirect antimicrobial effects by enhancing lymphocyte proliferation, antibody production, cytokine release, and immunomodulation, as well as stimulating nitric oxide (NO) generation [13], [14].

Hydrogen peroxide, a natural antibacterial agent, is widely used to clean wounds. This chemical is believed to play a crucial role in honey's ability to inhibit bacterial growth. However, the concentration of hydrogen peroxide commonly utilized in wound care is more harmful than that found in honey. The concentration of peroxide in honey is significantly lower and more compatible with cells, yet it still effectively inhibits bacterial development [37], [38]. Honey's anti-inflammatory properties also limit the synthesis of plasminogen activator inhibitor (PAI) by macrophages [15]. PAI prevents the conversion of plasminogen, an enzymatically inactive precursor of plasmin, into active plasmin. Inflammation promotes PAI development, hence honey's method for reducing PAI synthesis is most likely connected to its anti-inflammatory properties [39]. Several studies, both in vitro and in vivo, have demonstrated that various types of honey are effective against a wide range of bacteria, including those commonly associated with wound and burn infections, such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Acinetobacter baumannii*, and *Staphylococcus epidermidis*. Honey's high viscosity creates a protective barrier against infection [14].

Antimicrobial peptides and phenols produced from honey have been shown to inhibit bacterial growth. They are particularly effective at inhibiting biofilm development in a variety of bacterial species, including *Staphylococcus aureus*, *Escherichia coli*, and *Proteus mirabilis*, which typically use biofilm as a resistance mechanism. A 0.5% honey concentration also helps prevent inter-bacterial communication, known as quorum sensing. This pathway is critical for controlling bacterial virulence and resistance. Honey can also suppress the expression of essential virulence genes, such as fibronectin-binding proteins in *Streptococcus pyogenes* and curli genes (csgBAC), as well as quorum-sensing genes (including AI-2 importers and indole biosynthesis) and virulence genes (such as LEE genes) in *Escherichia coli* [40], [41].

4.3. Benefits of medical grade honey (MGH) on the wound healing process

Previous research has shown that honey dressings make a substantial difference in improving wound healing. This review revealed honey dressings as a wound care method, with the result that complete epithelialization of lateral palatal defects was clinically evident in 66.7% of test group participants 2 weeks following surgery [18]. Honey treatment promotes early epithelialization of palatal surgical wounds following palate repair and lowers the risk of palatal fistulas [18]. A Case Series investigation discovered that medical grade honey (MGH) provides a moist wound environment, accelerates autolytic debridement, exhibits anti-inflammatory activity, and promotes angiogenesis and re-epithelialization [25], resulting in significantly faster healing up to day 42 post-caesarean section [23]. MGH can also reduce bacterial burden, lower the risk of infection, and improve healing outcomes [28]. Furthermore, incubating honey with the strongest wound exudate causes considerable degradation of the GOX enzyme, a quick and potent H₂O₂ producer [31]. Honey improves surgical results and shortens recovery time [21].

The wound healing process involves 38 types of wounds worldwide, affecting the epidemiology and economic impact on healthcare systems. Treating wounds includes reducing inflammation, preventing infection, edema, and edema, enhancing cell synthesis, and increasing DNA damage in the wound. Honey, a type of wound treatment, has antibacterial and anti-inflammatory properties, which help prevent skin damage and inflammation. It also treats diabetic wounds, preventing complications like amputation or infection [17]. Royal jelly, a natural supplement, has been found to enhance skin wound healing by modulating Glutathione Peroxidase activity and CCL2 chemokine gene transcription. This treatment can effectively reduce wound healing time and costs compared to paraffin and povidone-iodine [42]. Honey's anti-inflammatory properties include the inhibition of plasminogen activator inhibitor (PAI) synthesis by macrophages, which facilitates fibrinolysis and eschar reduction. In vitro and in vivo studies demonstrate that honey reduces COX-1 and COX-2 activity, interfering with prostaglandin synthesis and thereby decreasing edema and improving oxygen and nutrient availability for tissue repair [42]-[45].

4.4. Recommendations for using honey as a wound care alternative

According to the review, honey can be utilized as an alternative treatment for wounds. A case series analysis suggested that honey may serve as an alternative or complementary treatment for wound healing [25]. Honey is also used for financial reasons, as quantitative studies have shown that it is a cost-effective and straightforward alternative for treating persistent wound infections [26]. According to Koloh *et al.* [29], chestnut honey is an alternative treatment for resistant infections and chronic wounds. Another advantage of honey dressings is their ease of use, as honey is a practical, simple, and inexpensive way to heal wounds in a variety of orthopedic diseases, including those with exposed bones or tendons [15]. The findings of this systematic review support the use of medical-grade honey (MGH) as an effective alternative treatment to antibiotics and povidone-iodine, while also accelerating recovery [23]. Furthermore, honey has been shown to expedite wound healing, resulting in a quicker recovery time and lower post-operative morbidity [20].

Honey contains several antioxidants, including flavonoids, monophenols, polyphenols, vitamin C, and methylsyringate, which inhibit the amplification of inflammation caused by reactive oxygen species (ROS). These antioxidants are responsible for the method that honey uses to alleviate wound pain [35]. Honey, in addition to being a solution high in sugar, is also a biological wound dressing that contains many bioactive components that can stimulate wound healing through various pathways. Honey can speed up the healing process of wounds by working on the three phases of growth: proliferation, remodelling, and inflammation. Honey is known to enhance the production of collagen, as well as angiogenesis and granulation tissue creation. Additionally, honey boosts wound contraction and promotes epithelialization [46]. In addition to alleviating pain and removing odor from the area, honey also has a debridement effect, meaning it removes debris from the lesion [15]. Allergies to honey are rare, but allergic reactions to honey proteins and allergens are possible.

4.5. Heterogeneity across studies

A critical consideration is the substantial heterogeneity observed across the included studies. Variations in honey types (Manuka, chestnut, heather, medical-grade), concentrations, wound types (surgical, chronic, diabetic, pressure ulcers), patient populations, and outcome measures limit the ability to draw definitive conclusions regarding optimal protocols. The composition of honey varies significantly based on floral source and geographical origin, which may account for differences in therapeutic efficacy. This variability underscores the need for standardized honey products and treatment protocols in future research.

4.6. Public health, policy, and economic implications

Honey's affordability and accessibility make it particularly relevant for wound care in LMICs and rural areas, where access to advanced wound care products is often limited [15]. Medical-grade honey products have demonstrated cost-effectiveness compared to conventional dressings in several studies [26]. The cultural familiarity of honey as a traditional medicine across many communities worldwide may improve patient adherence and acceptance, particularly in settings where modern wound care products are perceived as foreign or inaccessible [15].

From a policy perspective, the growing evidence base supports consideration of honey-based therapies for inclusion in national wound care guidelines and potentially in WHO essential wound care recommendations. Integration of honey into community health promotion programs, school health first-aid protocols, and occupational health programs for agricultural and industrial workers in underserved areas could extend the reach of effective wound care [15].

The relevance of honey-based wound care extends across populations, including elderly patients with chronic wounds, diabetic patients with foot ulcers and pressure sores [24], [47], and pediatric populations requiring safe and acceptable wound care options [48], [49]. However, specific evidence for pediatric populations remains limited and warrants further investigation.

5. CONCLUSION

This systematic review demonstrates that honey, particularly medical-grade honey, shows considerable promise as an alternative wound healing therapy with antimicrobial, anti-inflammatory, and tissue-regenerating properties. The evidence supports its efficacy across diverse wound types including surgical, chronic, diabetic, and infected wounds. However, the current evidence base is limited by study heterogeneity, small sample sizes, variability in honey types and protocols, and the predominance of studies from high-income settings.

The findings cannot be generalized without caution, particularly to populations and settings underrepresented in the current literature. While honey-based therapies offer a cost-effective and culturally acceptable approach to wound care, the evidence is not yet sufficient to recommend their routine use as a

standalone replacement for conventional treatments. Rather, honey should be considered as a complementary therapy within an integrated wound management approach.

Healthcare practitioners should consider medical-grade honey products as adjunctive therapy in wound care, particularly in settings where conventional treatments are costly or unavailable. Family engagement and culturally sensitive approaches to wound care education should be incorporated into practice. Clinicians should be aware of the variability in honey products and preferentially use standardized, medical-grade formulations.

Future research should prioritize large-scale, multi-center randomized controlled trials with standardized honey products, treatment protocols, and outcome measures (healing time, infection rates, pain scores, cost-effectiveness) to enable quantitative synthesis and guideline development. Comparative studies across different honey types and concentrations, investigations in diverse clinical settings including LMICs, and studies specifically addressing pediatric, geriatric, and diabetic populations are needed.

REFERENCES

- [1] E. M. Tottoli, R. Dorati, I. Genta, E. Chiesa, S. Pisani, and B. Conti, "Skin wound healing process and new emerging technologies for skin wound care and regeneration," *Pharmaceutics*, vol. 12, no. 8, p. 735, Aug. 2020, doi: 10.3390/pharmaceutics12080735.
- [2] H. Ding, Z. Yu, H. Yao, X. Xu, Y. Liu, and M. Chen, "Global burden and trends of disability-adjusted life years and mortality for decubitus ulcer: a systematic analysis," *International Wound Journal*, vol. 21, no. 2, Feb. 2024, doi: 10.1111/iwj.14604.
- [3] D. Balderas-Cordero, O. Canales-Alvarez, R. Sánchez-Sánchez, A. Cabrera-Wrooman, M. M. Canales-Martinez, and M. A. Rodriguez-Monroy, "Anti-inflammatory and histological analysis of skin wound healing through topical application of Mexican propolis," *International Journal of Molecular Sciences*, vol. 24, no. 14, p. 11831, Jul. 2023, doi: 10.3390/ijms241411831.
- [4] World Health Organization (WHO), "Sepsis, key facts." [Online]. Available: <https://www.who.int/news-room/fact-sheets/detail/sepsis>.
- [5] D. G. Armstrong, M. A. Swerdlow, A. A. Armstrong, M. S. Conte, W. V. Padula, and S. A. Bus, "Five year mortality and direct costs of care for people with diabetic foot complications are comparable to cancer," *Journal of Foot and Ankle Research*, vol. 13, no. 1, Jan. 2020, doi: 10.1186/s13047-020-00383-2.
- [6] C. K. Sen, "Human wound and its burden: updated 2025 compendium of estimates," *Advances in Wound Care*, vol. 14, no. 9, pp. 429–438, Sep. 2025, doi: 10.1177/21621918251359554.
- [7] C. C. F. Pleeing, F. A. D. T. G. Wagener, H. de Rooster, and N. A. J. Cremers, "Revolutionizing non-conventional wound healing using honey by simultaneously targeting multiple molecular mechanisms," *Drug Resistance Updates*, vol. 62, p. 100834, May 2022, doi: 10.1016/j.drug.2022.100834.
- [8] R. Hossain *et al.*, "Propolis: an update on its chemistry and pharmacological applications," *Chinese Medicine*, vol. 17, no. 1, p. 100, Aug. 2022, doi: 10.1186/s13020-022-00651-2.
- [9] X. Lan *et al.*, "Global, regional, and national burden of pressure ulcers from 1990 to 2021 and projections over the next decade: results from the 2021 GBD study," *Wound Repair and Regeneration*, vol. 33, no. 4, Jul. 2025, doi: 10.1111/wrr.70064.
- [10] World Health Organization (WHO), "Sepsis symptoms, overview sepsis, treatment." [Online]. Available: <https://www.who.int/health-topics/sepsis>.
- [11] K. E. Rudd *et al.*, "Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study," *The Lancet*, vol. 395, no. 10219, pp. 200–211, Jan. 2020, doi: 10.1016/S0140-6736(19)32989-7.
- [12] E. Tacconelli *et al.*, "Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis," *The Lancet Infectious Diseases*, vol. 18, no. 3, pp. 318–327, Mar. 2018, doi: 10.1016/S1473-3099(17)30753-3.
- [13] J. Y. Mielles, C. Vyas, E. Aslan, G. Humphreys, C. Diver, and P. Bartolo, "Honey: an advanced antimicrobial and wound healing biomaterial for tissue engineering applications," *Pharmaceutics*, vol. 14, no. 8, p. 1663, 2022, doi: 10.3390/pharmaceutics14081663.
- [14] H. Scephankova *et al.*, "Role of honey in advanced wound care," *Molecules*, vol. 26, no. 16, p. 4784, Aug. 2021, doi: 10.3390/molecules26164784.
- [15] A.-S. A.-A. Ahmed, S. Eltrejy, and M. I. Kandil, "Honey dressing: a missed way for orthopaedic wound care," *International Orthopaedics*, vol. 46, no. 11, pp. 2483–2491, Nov. 2022, doi: 10.1007/s00264-022-05540-9.
- [16] Y. Tang, L. Chen, and X. Ran, "Efficacy and Safety of Honey Dressings in the management of chronic wounds: an updated systematic review and meta-analysis," *Nutrients*, vol. 16, no. 15, p. 2455, Jul. 2024, doi: 10.3390/nu16152455.
- [17] E. Yildiz Karadeniz and E. Kaplan Serin, "Use of honey in diabetic foot ulcer: systematic review and meta-analysis," *Journal of Tissue Viability*, vol. 32, no. 2, pp. 270–278, May 2023, doi: 10.1016/j.jtv.2023.03.002.
- [18] A. A. Adekunle, O. James, E. O. Onuoha, and W. L. Adeyemo, "Wound healing following palatoplasty using either honey or warm saline mouth bath for postoperative wound care: a randomized-controlled study," *The Cleft Palate Craniofacial Journal*, vol. 60, no. 8, pp. 962–970, Aug. 2023, doi: 10.1177/10556656221086192.
- [19] E. O. Onuoha, A. A. Adekunle, S. O. Ajike, O. M. Gbotolorun, and W. L. Adeyemo, "Effect of Manuka honey socket dressing on postoperative sequelae and complications following third molar extraction: a randomized controlled study," *Journal of Cranio-Maxillofacial Surgery*, vol. 51, no. 4, pp. 252–260, Apr. 2023, doi: 10.1016/j.jcms.2023.05.001.
- [20] M. Alasqah, A. Alrashidi, N. Alshammari, A. Alshehri, and K. Gufran, "Effect of honey dressing material on palatal wound healing after harvesting a free gingival graft: a prospective randomized case control study," *European Review for Medical & Pharmacological Sciences*, vol. 26, no. 8, pp. 2662–2668, 2022.
- [21] V. Salehi *et al.*, "Does application of honey improve surgical outcome in pilonidal cyst excision with secondary intention healing? A prospective randomized placebo-controlled clinical trial," *Perioperative Medicine*, vol. 11, no. 1, p. 1, Dec. 2022, doi: 10.1186/s13741-021-00237-w.
- [22] H. C. Guthrie *et al.*, "A pre-clinical evaluation of silver, iodine and Manuka honey based dressings in a model of traumatic extremity wounds contaminated with *Staphylococcus aureus*," *Injury*, vol. 45, no. 8, pp. 1171–1178, 2014, doi: 10.1016/j.injury.2014.05.007.
- [23] A. Bocoum *et al.*, "EP323 medical grade honey enhances the healing of Caesarean section wounds and does not compromise in the prevention of infections when compared to antibiotics combined with povidone-iodine -- a prospective controlled trial," *Journal of Wound Management*, vol. 24, no. 2, p. 210, 2023.
- [24] G. E. Papanikolaou, G. Gousios, and N. A. J. Cremers, "Use of medical-grade honey to treat clinically infected heel pressure ulcers in high-risk patients: a prospective case series," *Antibiotics*, vol. 12, no. 3, p. 605, Mar. 2023, doi: 10.3390/antibiotics12030605.

- [25] G. Papanikolaou, G. Gousios, and N. Cremers, "EP096 use of medical grade honey in the management of heel pressure ulcers: a case series," *Journal of Wound Management*, vol. 24, no. 2, p. 84, 2023.
- [26] D. Chrysostomou, A. Pokorna, and N. Cremers, "EP186 medical grade honey, an alternative to decrease bacterial load in the wound bed," *Journal of Wound Management*, vol. 24, no. 2, p. 133, 2023.
- [27] O. E. Agbagwa, C. Ekeke, and P. C. Israel, "Antibacterial efficacy and healing potential of honey from different zones in Nigeria on diabetic-induced wound infection in wistar rats," *International Journal of Microbiology*, vol. 2022, pp. 1–12, Oct. 2022, doi: 10.1155/2022/5308435.
- [28] C. McArdle, S. Coyle, and D. Santos, "The impact of wound pH on the antibacterial properties of medical grade honey when applied to bacterial isolates present in common foot and ankle wounds. An in vitro study," *Journal of Foot and Ankle Research*, vol. 16, no. 1, Jan. 2023, doi: 10.1186/s13047-023-00653-9.
- [29] R. Koloh *et al.*, "Chestnut honey is effective against mixed biofilms at different stages of maturity," *Antibiotics*, vol. 13, no. 3, p. 255, Mar. 2024, doi: 10.3390/antibiotics13030255.
- [30] R. Angioi, L. Holland, A. Morrin, and B. White, "EP371 honey antimicrobial properties: is there only room for Manuka honey?," *Journal of Wound Management*, vol. 24, no. 2, p. 239, 2023.
- [31] J. Majtan, V. Bugarova, M. Bucekova, J. Godocikova, and J. Farkasovska, "EP320 antibacterial efficacy of honey in proteolytic wound-like environment," *Journal of Wound Management*, vol. 24, no. 2, p. 209, 2023.
- [32] T. M. Magdas, M. David, A. R. Hategan, G. A. Filip, and D. A. Magdas, "Geographical origin authentication—a mandatory step in the efficient involvement of honey in medical treatment," *Foods*, vol. 13, no. 4, p. 532, Feb. 2024, doi: 10.3390/foods13040532.
- [33] P. Barazesh, H. Hajihassani, F. Motalebi, S. M. H. Neiresi, R. Hajihassani, and A. R. Mehrabian, "Unlocking the healing potential: a comprehensive review of ecology and biology of medical-grade honey in wound management and tissue regeneration," *Health Science Reports*, vol. 8, no. 1, Jan. 2025, doi: 10.1002/hsr2.70240.
- [34] A. H. Rahmani and A. Y. Babiker, "Review on role of honey in disease prevention and treatment through modulation of biological activities," *Open Life Sciences*, vol. 20, no. 1, Mar. 2025, doi: 10.1515/biol-2025-1069.
- [35] A. S. Lubis *et al.*, "The effect of honey on post-tonsillectomy pain relief: a randomized clinical trial," *Brazilian Journal of Otorhinolaryngology*, vol. 89, no. 1, pp. 60–65, Jan. 2023, doi: 10.1016/j.bjorl.2021.08.007.
- [36] A. Naskar *et al.*, "Mechanistic roles of different varieties of honey on wound healing: recent update," *Journal of Pharmacology and Pharmacotherapeutics*, vol. 15, no. 1, pp. 5–18, Mar. 2024, doi: 10.1177/0976500X241237361.
- [37] S. R. Hewett, S. D. Crabtree, E. E. Dodson, C. A. Rieth, R. M. Tarkka, and K. Naylor, "Both Manuka and non-Manuka honey types inhibit antibiotic resistant wound-infecting bacteria," *Antibiotics*, vol. 11, no. 8, 2022, doi: 10.3390/antibiotics11081132.
- [38] A. Gościński, E. Attard, I. J. Malesza, A. Kamiński, and J. Cielecka-Piontek, "Modern honey-based delivery systems for wound healing: a review of current trends and future perspectives," *Applied Sciences*, vol. 15, no. 18, 2025, doi: 10.3390/app15189997.
- [39] N. E. F. Esa *et al.*, "A review on recent progress of stingless bee honey and its hydrogel-based compound for wound care management," *Molecules*, vol. 27, no. 10, p. 3080, May 2022, doi: 10.3390/molecules27103080.
- [40] J.-H. Lee *et al.*, "Low concentrations of honey reduce biofilm formation, quorum sensing, and virulence in *Escherichia coli* O157:H7," *Biofouling*, vol. 27, no. 10, pp. 1095–1104, Nov. 2011, doi: 10.1080/08927014.2011.633704.
- [41] G. M. Hilliard, T. S. Wilkinson, L. G. Harris, R. E. Jenkins, and L. P. Shormick, "PCL-gelatin honey scaffolds promote *Staphylococcus aureus* agrA expression in biofilms with *Pseudomonas aeruginosa*," *Frontiers in Microbiology*, vol. 15, Sep. 2024, doi: 10.3389/fmicb.2024.1440658.
- [42] K. L. Suryadinata, A. Basuki, A. Song, N. V. Yovita, A. P. Pakan, and A. E. Sagala, "Effect of honey and povidone-iodine on acute laceration wound healing: a pilot randomised controlled trial study," *Journal of Wound Care*, vol. 33, no. 8, pp. 570–576, Aug. 2024, doi: 10.12968/jowc.2022.0020.
- [43] M. S. Ghashghaie, M. Ebrahimi, and M. Eidi, "Royal jelly enhances skin wound healing in mice model by modulating glutathione peroxidase activity and CCL2 chemokine gene transcription," *Journal of Advances in Medical and Biomedical Research*, vol. 32, no. 151, pp. 154–162, Mar. 2024, doi: 10.61186/jambr.32.151.154.
- [44] C. I. MacInnis, B. A. Keddie, and S. F. Pernal, "Honey bees with a drinking problem: potential routes of *Nosema ceranae* spore transmission," *Parasitology*, vol. 149, no. 5, pp. 573–580, Nov. 2022, doi: 10.1017/S0031182021001827.
- [45] N. Navaei-Alipour, M. Mastali, G. A. Ferns, M. Saberi-Karimian, and M. Ghayour-Mobarhan, "The effects of honey on pro- and anti-inflammatory cytokines: a narrative review," *Phytotherapy Research*, vol. 35, no. 7, pp. 3690–3701, Jul. 2021, doi: 10.1002/ptr.7066.
- [46] A. Iosageanu, L. M. Stefan, O. Craciunescu, and A. Cimpean, "Anti-inflammatory and wound healing properties of different honey varieties from Romania and correlations to their composition," *Life*, vol. 14, no. 9, p. 1187, Sep. 2024, doi: 10.3390/life14091187.
- [47] E. Majid, S. Pathan, B. F. Zuberi, M. Rehman, and S. Malik, "Comparison of honey & povidone iodine dressings in post-caesarean surgical site wound infection healing," *Pakistan Journal of Medical Sciences*, vol. 39, no. 6, pp. 1803–1808, Sep. 2023, doi: 10.12669/pjms.39.6.7499.
- [48] E. Smaropoulos and N. A. J. Cremers, "Treating severe wounds in pediatrics with medical grade honey: a case series," *Clinical Case Reports*, vol. 8, no. 3, pp. 469–476, Mar. 2020, doi: 10.1002/ccr3.2691.
- [49] M. Moniruzzaman, A. R. Khan, M. A. Haq, R. A. Naznin, and M. Haque, "Pediatric first-degree burn management with honey and 1% silver sulfadiazine (Ag-SD): comparison and contrast," *Cureus*, Dec. 2022, doi: 10.7759/cureus.32842.

APPENDIX

Table 1. Characteristics of included studies

No.	Author and year	Study design	Wound type	Honey type	Key findings	JB1 quality appraisal
1	Adekunle <i>et al.</i> (2022) [18]	Randomized controlled trial	Surgical (palatoplasty)	Natural honey	Honey facilitated prompt epithelialization of palatal surgical wounds and reduced the incidence of palatal fistulas. Complete epithelialization in 66.7% of test group at 2 weeks.	JB1 RCT checklist: 11/13 criteria met.

Table 1. Characteristics of included studies (continued)

No.	Author and year	Study design	Wound type	Honey type	Key findings	JBİ quality appraisal
2	Onuoha <i>et al.</i> (2023) [19]	Randomized controlled trial	Surgical (third molar extraction)	Manuka honey	Manuka honey accelerated healing of extraction sockets and significantly reduced complication rates compared to control.	JBİ RCT checklist: 10/13 criteria met.
3	Alasqah <i>et al.</i> (2022) [20]	Prospective randomized case-control study	Surgical (free gingival graft donor site)	Natural honey	Honey accelerated wound healing, resulting in shorter recovery duration and reduced post-operative morbidity.	JBİ RCT checklist: 9/13 criteria met.
4	Salehi <i>et al.</i> (2022) [21]	Prospective randomized placebo-controlled clinical trial	Surgical (pilonidal cyst excision)	Natural honey	Honey application improved surgical outcomes with secondary wound healing, shortening recovery period and time to resume regular activities.	JBİ RCT checklist: 10/13 criteria met
5	Guthrie <i>et al.</i> (2014) [22]	Randomized controlled trial	Traumatic extremity wounds (contaminated)	Manuka honey	Iodine and Manuka honey-based dressings minimized bacterial burden on extensively contaminated soft tissue wounds, particularly when surgical treatment was delayed.	JBİ RCT checklist: 9/13 criteria met.
6	Bocoum <i>et al.</i> (2023) [23]	Prospective controlled trial	Surgical (Caesarean section)	Medical grade honey (MGH)	MGH demonstrated substantially faster healing up to day 42 post-surgery. Effective alternative to antibiotics and povidone-iodine.	JBİ quasi-experimental checklist: 7/9 criteria met.
7	Papanikolaou <i>et al.</i> (2023) [24]	Prospective case series	Chronic (infected heel pressure ulcers)	Medical grade honey (MGH, L-Mesitran)	Wounds treated with MGH resolved infections within 3–4 weeks and healed completely without complications. Recommended as alternative/complementary treatment.	JBİ case series checklist: 8/10 criteria met.
8	Papanikolaou <i>et al.</i> (2023) [25]	Case series	Chronic (Heel pressure ulcers)	Medical grade honey (MGH)	MGH created moist wound environment, accelerated autolytic debridement, exhibited anti-inflammatory properties, and promoted angiogenesis and re-epithelialization.	JBİ case series checklist: 7/10 criteria met.
9	Ahmed <i>et al.</i> (2022) [15]	Case series / clinical review	Orthopaedic wounds (including exposed bones/tendons)	Natural honey	Honey served as an efficient, straightforward, and economical wound treatment for various orthopaedic disorders.	JBİ case series checklist: 6/10 criteria met.
10	Chrysostomou <i>et al.</i> (2023) [26]	Case series	Chronic (Persistent wound infections)	Medical grade honey (MGH)	Following local MGH therapy, bacterial load diminished; in certain instances cultures were sterile. MGH is cost-effective and user-friendly alternative.	JBİ case series checklist: 7/10 criteria met.
11	Agbagwa <i>et al.</i> (2022) [27]	Experimental Study	Diabetic wounds (animal model)	Moringa-infused Nigerian honey	Honey infused with moringa exhibited superior efficacy and faster healing of diabetic wounds compared to other honey variants and silver sulfadiazine.	JBİ quasi-experimental checklist: 6/9 criteria met.
12	McArdle <i>et al.</i> (2023) [28]	In Vitro Study	Foot and ankle wound isolates	Medical grade honey (MGH)	MGH may be used on non-infected foot/ankle wounds to minimize germs, reduce infection likelihood, and improve healing. Wound pH influences antibacterial efficacy.	JBİ cross-sectional checklist: 6/8 criteria met.
13	Koloh <i>et al.</i> (2024) [29]	In Vitro Study	Mixed biofilms (wound-relevant bacteria)	Chestnut honey	Chestnut honey suppressed early and moderately mature mixed biofilms, limiting bacterial growth and biofilm development. Alternative treatment for resistant infections.	JBİ cross-sectional checklist: 6/8 criteria met.

Table 1. Characteristics of included studies (continued)

No.	Author and year	Study design	Wound type	Honey type	Key findings	JBİ quality appraisal
14	Angioi <i>et al.</i> (2023) [30]	In Vitro Study	Wound-related bacterial isolates	Heather honey	Heather honey demonstrated potential as an antibacterial agent for incorporation into honey-infused wound dressing compositions.	JBİ cross-sectional checklist: 5/8 criteria met.
15	Majtan <i>et al.</i> (2023) [31]	In Vitro Study	Proteolytic wound-like environment	Various honey types	Incubation of honey with potent wound exudate resulted in considerable degradation of the GOX enzyme, a quick and efficient H ₂ O ₂ producer. Implications for clinical honey selection.	JBİ cross-sectional checklist: 6/8 criteria met.
16	Magdas <i>et al.</i> (2024) [32]	Analytical study	N/A (honey characterization)	Multiple honey types (geographical origin)	Honey is a complex matrix of over 200 chemicals with significant compositional variations based on geographical origin. Authentication is essential for medical use.	JBİ cross-sectional checklist: 8/8 criteria met.

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